

Rhodium-Catalyzed Asymmetric Addition of Potassium Organotrifluoroborates to *N*-Sulfonyl Ketimines

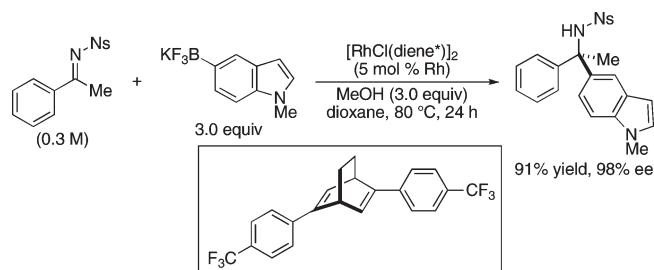
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ABSTRACT



A rhodium-catalyzed asymmetric addition of readily available potassium organotrifluoroborates to both *N*-tosyl and *N*-nosyl ketimines has been developed. High enantioselectivity has been achieved by using a chiral diene ligand, and the nosyl group of the addition products can be easily removed while retaining the enantiomeric purity.

Transition-metal-catalyzed asymmetric addition of organometallic reagents to imines is one of the most powerful methods for the construction of enantioenriched chiral amines possessing an α -carbon stereocenter.¹ Most of the existing methods in this regard employ aldimines as substrates under the catalysis of copper,² zirconium,³ rhodium,⁴ or palladium.⁵ In contrast, asymmetric additions to ketimines have been much less explored,⁶ and to the best of our knowledge, only the copper-catalyzed addition of an allylboronate⁷ and the copper-⁸ or zirconium-catalyzed⁹ addition of dialkylzincs have been known until recently.¹⁰ To broaden the scope of the applicable

organometallic nucleophiles, we reported a rhodium-catalyzed asymmetric addition of sodium tetraarylborates

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to *N*-tosyl ketimines in the presence of a chiral diene ligand in 2010.^{11,12} Although high yield and enantioselectivity were achieved, the major drawback of this process in a synthetic point of view was the requirement to use tetraarylborates¹³ to promote the reaction effectively. In addition, the use of *N*-nosyl ketimines resulted in moderate yields under this catalytic system. To overcome these problems, herein we describe that readily available potassium organotrifluoroborates^{14,15} can now be employed as the nucleophile for the rhodium-catalyzed asymmetric addition to both *N*-tosyl and *N*-nosyl ketimines.

As we have previously reported,¹¹ a reaction of *N*-tosyl imine of 4'-chloroacetophenone (**1a**; 0.2 M initial concentration) with sodium tetraphenylborate (2.0 equiv) smoothly proceeds in the presence of [RhCl((*R,R*)-**L1**)]₂ (5 mol % Rh) and MeOH (2.0 equiv) in dioxane at 60 °C to give addition product (*S*)-**2a** in 83% yield with 97% ee (eq 1). Under these conditions, the use of potassium phenyltrifluoroborate in place of sodium tetraphenylborate significantly lowered the reactivity, giving **2a** only in 36% yield, although the enantioselectivity stayed high (98% ee). After some investigation of the reaction conditions, we were able to find a set of conditions that can efficiently promote this reaction. Thus, as shown in Table 1, entry 1, addition product **2a** can be obtained in 84% yield with 98% ee by reacting **1a** (0.3 M initial concentration) with potassium phenyltrifluoroborate (3.0 equiv)

in the presence of [RhCl((*R,R*)-**L1**)]₂ (5 mol % Rh) and MeOH (3.0 equiv) in dioxane at 80 °C.

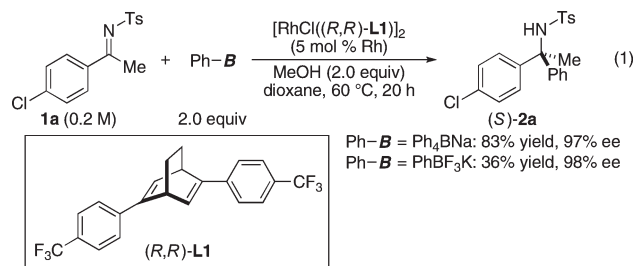


Table 1. Rhodium-Catalyzed Asymmetric Addition of Potassium Phenyltrifluoroborate to *N*-Tosyl and *N*-Nosyl Ketimines **1**

entry	substrate	product	yield (%) ^a	ee (%) ^b
1	1a	(<i>S</i>)- 2a	84	98
2	1b : X = H	(<i>S</i>)- 2b : X = H	97	>99.5
3	1c : X = Cl	(<i>S</i>)- 2c : X = Cl	95	>99.5
4 ^c	1d	(<i>S</i>)- 2d	88	99
5	1e : Ar = 4-ClC ₆ H ₄	(<i>S</i>)- 2e : Ar = 4-ClC ₆ H ₄	91	95
6 ^{c,d}	1f : Ar = 4-MeC ₆ H ₄	(<i>S</i>)- 2f : Ar = 4-MeC ₆ H ₄	80	95
7 ^{c,d,e}	1g : Ar = 3-MeC ₆ H ₄	(<i>S</i>)- 2g : Ar = 3-MeC ₆ H ₄	76	93
8 ^{c,d}	1h : Ar = 2-naphthyl	(<i>S</i>)- 2h : Ar = 2-naphthyl	77	92
9	1i : Ar = 2-furyl	(<i>S</i>)- 2i : Ar = 2-furyl	71	95

^a Isolated yield. ^b Determined by chiral HPLC with hexane/2-propanol. ^c The reaction was conducted at 90 °C. ^d The reaction was conducted for 48 h. ^e The reaction was conducted with 4.0 equiv of PhBF₃K and 4.0 equiv of MeOH.

Under these newly established conditions, several other *N*-tosyl ketimines **1b–1d** effectively undergo phenylation to give products **2** in high yields with excellent enantioselectivities (88–97% yield, ≥99% ee; entries 2–4). Furthermore, in contrast to our previous reactions using sodium tetraarylborates as the nucleophile,¹¹ the present catalysis is also effective for the reaction of *N*-nosyl ketimines. For example, *N*-nosyl imines of various (hetero)aryl

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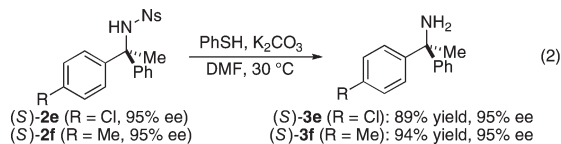
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methyl ketones (**1e–1i**) are efficiently converted to phenyl-lation products **2** in good to excellent yields with high ee (71–91% yield, 92–95% ee; entries 5–9). Of course, the nosyl group of the products thus obtained can be readily deprotected under mild reaction conditions while retaining the enantiomeric excesses as demonstrated in eq 2.¹⁷



With regard to the nucleophilic component, various potassium aryltrifluoroborates including 2-naphthyl- and 5-indolylborates can be used in the reaction with *N*-nosyl imine of acetophenone (**1j**) to give the corresponding adducts **2** in high yield with $\geq 95\%$ ee (Table 2, entries 1–7).¹⁸ In addition to these aryl nucleophiles, an alkenyltrifluoroborate can also be employed to form a highly

Table 2. Rhodium-Catalyzed Asymmetric Addition of Potassium Organotrifluoroborates to *N*-Nosyl Ketimine **1j**

entry	R	product	yield (%) ^a	ee (%) ^b
1		(<i>R</i>)- 2j	80	98
2		(<i>R</i>)- 2f	79	98
3 ^c		(<i>R</i>)- 2k	78	96
4 ^c		(<i>R</i>)- 2l	80	95
5		(<i>R</i>)- 2g	82	95
6 ^d		(<i>R</i>)- 2h	86	96
7		(<i>R</i>)- 2m	91	98
8		(<i>S</i>)- 2n	80	97

^a Isolated yield. ^b Determined by chiral HPLC with hexane/2-propanol. ^c The reaction was conducted for 48 h at 90 °C. ^d The reaction was conducted for 48 h at 100 °C.

substituted allylamine derivative with high enantioselectivity (entry 8). This example also highlights the advantage

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(18) Potassium trifluoroborates of 4-methoxycarbonylphenyl, 3-thienyl, and 2-furyl are not suitable nucleophiles in the present catalysis.

of using potassium organotrifluoroborates over sodium tetraarylborates.¹⁹

The stereochemical outcome in the reaction of **1a** with potassium phenyltrifluoroborate under the catalysis of Rh/(*R,R*)-**L1** can be rationalized as follows (Figure 1). To minimize the unfavorable steric interaction between the sulfonyl moiety on the nitrogen of **1a** and the aryl group on the olefin of (*R,R*)-**L1**, **1a** approaches phenylrhodium species with its *si*-face, thereby leading to the formation of **2a** with an *S* configuration.^{4c,f}

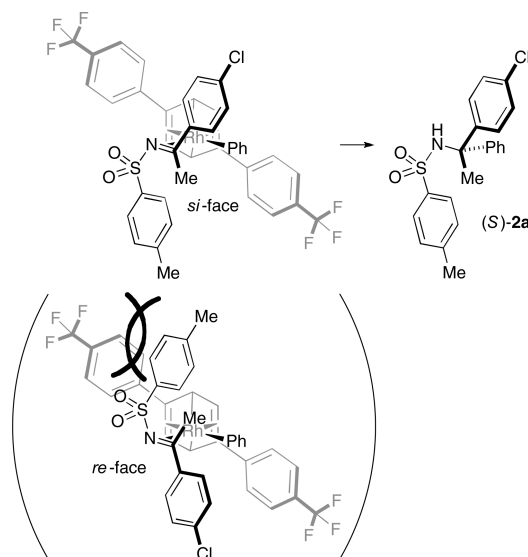


Figure 1. Proposed stereochemical pathway for the rhodium-catalyzed addition of potassium phenyltrifluoroborate to **1a**.

In summary, we have disclosed that readily available potassium organotrifluoroborates can be employed as the nucleophile for the rhodium-catalyzed asymmetric addition to both *N*-tosyl and *N*-nosyl ketimines. High enantioselectivity has been achieved by using chiral diene (*R,R*)-**L1** as the ligand, and the nosyl group of the addition products can be easily removed while retaining the enantiomeric purity.

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Supporting Information Available. Experimental procedures and compound characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

(19) Attempts to prepare sodium tetraalkenylborates were unsuccessful (unpublished results).